UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,170	04/14/2004	Goran Bondjers	133087.08211(100029-2PUS)	6354

52286 7590 05/09/2008

Pepper Hamilton LLP
400 Berwyn Park
899 Cassatt Road
Berwyn, PA 19312-1183

EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
05/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/824,170	BONDJERS ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *11,23 and 26-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 12-22, 24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/2008,4/18/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election of **Group I**, claims drawn to a **pharmaceutical combination** comprising a betablocker and an HMG-CoA reductase inhibitor, with **rosuvastatin ((E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl-(methylsulfonyl)-amino]-pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid)** as a **species** of HMG-CoA reductase inhibitor is acknowledged. Because applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Within elected Group I, claims 1-10, 12-22, 24 and 25 have been examined to the extent of Applicants' elected species. Claims 11, 23, 26-36 are withdrawn from consideration since they are non-elected invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10, 12-22, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scott (WO 99/11260) of record in view of Market letter (13 Dec. 1999).

Scott discloses that a pharmaceutical composition for a pharmaceutical kit comprising a combination of a lipid lowering agent, such as atorvastatin (a known statin as an HMG-CoA reductase inhibitor) in the effective amount and one beta blocker, metaprolol, with a pharmaceutically acceptable carrier or diluents, is useful for the treatment of atherosclerosis, combined hypertension and hyperlipidemia or symptoms

of cardiac risk in humans. (see abstract, page 8 lines 17-18, page 19 line 20, pages 34-39, claims 1, 18, 22, 45-46, 47-52).

Scott differs from Applicants claimed invention that Scott employs atorvastatin instead of Applicants' elected species, **rosuvastatin ((E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl-(methylsulfonyl)-amino]-pyrimidin-5-yl](3R,5S)-3,5-dihydroxyhept-6-enoic acid)** in the combination with metaprolol, and Scott does the teach the molar ratio of the combination set forth in claims 5,13,17, and 25.

Market letter teaches that ZD 4522 (rosuvastatin) is a “superstatin”, a second-generation HMG-CoA reductase inhibitor which is more potent than atorvastatin. Market letter teaches that ZD 4522(rosuvastatin) 40mg/day lowered low-density lipoprotein cholesterol levels by more than 60%, compared to 40mg/day atorvastatin (Lipitor), and also 10mg/day ZD 4522 (rosuvastatin) also substantially boosted high-density lipoprotein cholesterol levels, by 14% versus 10mg atorvastatin with the equivalent safety and tolerability. (page 3 bottom, under Challenging Lipitor with “superstatin” through page 4).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ rosuvastatin instead of atorvastatin in Scott’s combination for the treatment of atherosclerosis. One would have been motivated to make such a modification in order to achieve more potent effects in treating atherosclerosis patients disclosed by Scott. There would have been a reasonable expectation of successfully treating atherosclerosis with combination of rosuvastatin and metoprolol because Market letter teaches that rosuvastatin is more potent than

atorvastatin with equivalent safety and tolerability profile. Moreover, rosuvastatin is a superstatin compared to atorvastatin because it lowered low-density lipoprotein cholesterol levels by more than 60% and substantially boosted high density lipoprotein cholesterol levels by 14% compared to atorvastatin as taught by Market Letter. One would have been further motivated to employ rosuvastatin instead of atorvastatin in Scott's combination in order to achieve the beneficial effect of boosting the high density lipoprotein cholesterol level while effectively lowering the low-density lipoprotein cholesterol in patients suffering from atherosclerosis disclosed by Scott. With regard to the claimed ratio, as anyone of ordinary skill in the art will appreciate, preferred dosages and ratio of the active agents are merely exemplary and serve as useful guideposts for the physician. There are, however, many reasons for varying dosages, including by orders of magnitude; for instance, one having an unusually severe case of atherosclerosis would require a correspondingly higher dosages. Furthermore, it is routine during animal and clinical studies to dramatically vary dosage to obtain data on parameters such as toxicity. Therefore, the preferred dosages and amounts ratio of active agents to be used, the pharmaceutical forms, e.g., tablets, salts such as succinate, fumarate, etc; mode of administration, flavors, surfactant are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations and modes of administration.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/
Primary Examiner, Art Unit 1617

Jmk
May 7, 2008